

The role of anti-thyroglobulin antibody in treatment and follow up of differentiated thyroid cancer

The role of anti-thyroglobulin antibody in differentiated thyroid cancer

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Abstract

Aim: This study aimed to investigate the role of serum anti-thyroglobulin antibody (anti-TgAb) as a marker to predict the success of radioactive iodine (RAI) ablation therapy in differentiated thyroid cancer (DTC) patients and also investigate the role of anti-TgAb in the follow-up of thyroid cancer. **Materials and Methods:** One hundred thirteen DTC patients with total thyroidectomy who received RAI ablation therapy enrolled in this retrospective study. The first measurement was performed immediately before ablation therapy (thyroglobulin (Tg) 1, anti-TgAb 1). The second measurement was performed just before the whole-body iodine 131 (¹³¹I) scan (WBS) within 6–12 months after ablation (Tg 2, Anti-TgAb 2). Patients were divided into two groups according to ablation success: Group 1 (successful) and Group 2 (unsuccessful). Tg and anti-TgAb levels and the difference between two measurements were compared between groups. **Results:** In terms of Anti-Tg antibody positivity and the anti-Tg Ab 1 and anti-Tg Ab 2 levels, there was no statistically significant difference between groups ($p = 0.661$, $p = 0.716$, $p = 0.764$, respectively). When the groups were compared in terms of anti-Tg Ab level change after treatment, a statistically significant decrease was observed in Group 1 ($p < 0.001$), but there was no statistically significant decrease in Group 2 ($p = 0.277$). **Discussion:** In conclusion, a reduction in anti-Tg Ab level, measured within 6–12 months after the ablation, can be used as an indicator of treatment success.

Keywords

Anti-Thyroglobulin Antibody; Thyroglobulin; Differentiated Thyroid Cancer

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Introduction

Differentiated thyroid cancers are the most leading cause of endocrine tumors [1]. Globally, its incidence has increased in the last decades. Total thyroidectomy is the mainstay of management of thyroid cancers, and thereafter patients are treated with radioiodine therapy [2]. Traditionally, WBS, basal and TSH-induced serum Tg measurement and cervical ultrasonography (USG) are obtained for evaluating the disease recurrence [3]. Serum Tg level is a relevant indicator for monitoring DTC patients after total thyroidectomy with or without RAI therapy, and it is an indicator of cancer recurrence [4]. However, incorrect serum Tg may be detected in patients with serum anti-Tg Ab positive. For this reason, Tg cannot be an ideal tumor marker for the follow-up of those patients [5]. The percentages of anti-Tg Ab in DTC patients have been reported in the range of 10% to 30% [6]. There have been studies published recently on whether anti-Tg Ab positivity increases with the recurrence rate [4,7]. However, it is not entirely clear whether anti-Tg Ab is predictive response factor to treatment or plays any role in the follow-up of thyroid cancer [6, 8, 9,10]. The aim of our study was to examine the role of serum anti-Tg Ab as a marker for predicting RAI ablation therapy achievement in patients with DTC. The second purpose was to investigate the role of anti-Tg Ab in the follow-up of thyroid cancer.

Material and Methods

Patients

This retrospective study included 113 patients with total thyroidectomy who underwent ¹³¹I ablation therapy between 2003 and 2011 in our clinic. The inclusion criteria were as follows: 1)All patients had differentiated thyroid carcinoma type, 2) Patients had received empirical high-dose ¹³¹I ablation therapy after total thyroidectomy surgery, 3)Complete follow-up data for the 6-12 months postoperative visit. Subjects who had a non-differentiated cancer type were excluded from the study. Serum Tg and Anti-Tg antibody measurement
Serum Tg and anti-Tg Ab measurements were obtained under stimulated thyroid-stimulating hormone (TSH) condition. The first measurement was performed just before ablation therapy (Tg 1, anti-Tg Ab 1). The mean time duration between surgery and ablation therapy was 4.5±2.8 months. The second mea-

surement was performed just before WBS at 6-12 months after ablation (Tg 2, Anti-Tg Ab 2). Tg and Tg-Ab values were measured with immunoassay analysis by Abbott ARCHITECT i2000SR Analyzer (Abbott Diagnostics). Tg-Ab value above the reference range was accepted positive (normal Tg-Ab is <4.11 IU/ml).

Follow-up after RAI ablation

After 6-12 months of RAI ablation therapy, WBS was carried out under TSH stimulation. Concurrent Tg and anti-Tg Ab measurements were performed. Successful ablation was accepted when there was no residual or metastatic tissue in WBS and also Tg level <2 ng/ml. Subjects were assigned into two groups according to ablation success: Group 1 (successful) and Group 2 (unsuccessful).

Statistical analysis

Data obtained in the study were statistically evaluated using the SPSS 20.0 (Statistical Package for Social Sciences for Windows SSPS Inc, Chicago, IL, USA) program. Continuous variables were defined as a mean ± standard deviation or median values and also categorical variables were defined as absolute numbers. Between the groups, differences were evaluated with the independent-samples t-test or the Mann-Whitney test for continuous variables and the Chi-square or the Fisher's exact test for categorical variables. The Wilcoxon Signed-Rank test was used for analysis of the decrease in Tg and Anti-Tg Ab values. To evaluate correlation, the Spearman's correlation analysis was used. P <0.05 was accepted significant.

Results

Eleven of the 113 patients involved in the study were male and 102 of them were female. The ¹³¹I dose given to the patients was between 3.33-9.25GBq. The mean age was 46.73 ± 12.68 years. According to postoperative microscopic pathology results, 108 (96%) patients had papillary carcinoma and 5 (4%) patients had follicular carcinoma. The mean TSH values measured before the ablation therapy were 64.82 ± 34.72. There was lymph node metastasis in 7 (6%) patients and distant metastasis in 3 (3%) patients. In 103 (91%) patients, there was no metastasis. According to the treatment results, 88 (78%) patients were in Group 1 and 25 (22%) were in Group 2. There was no statistically significant difference between groups in terms

Table 1. Comparison of some clinical and demographic parameters

Characteristics		Group 1 (Successful) (n=88)	Group 2 (Unsuccessful) (n=25)	Total (n=113)	P
Age		46.88±11.62	46.20±16,14	46.73±12.68	0,675
Age subgroups	<45	39	11	50	0,977
	≥45	49	14	63	
Gender	Female	82	20	102	0,585
	Male	6	5	11	
Type of tumor	Papillary	83	25	108	0,064
	Follicular	5	0	5	
TSH level median (min-max)		63.22 (8.20-111.00)	72.87 (9.55-221.00)	63.63 (8.20-221.00)	0,792
Tumor Size mm median (min-max)		12.5 (1-70)	10.00 (1-45)	11.00 (1-70)	0.483

TSH: Thyroid-stimulating hormone

Table 2. Comparison of antithyroglobulin antibody and thyroglobulin between two groups

Variables		Group 1 (Successful)	Group 2 (Unsuccessful)	P
Anti-TgAb	positive	31	10	0.661
	negative	57	15	
Anti-Tg Ab 1 level median (min-max)		19.35 (4.21-177.19)	14.48 (6.12-221.01)	0.716
Anti-Tg Ab 2 level median (min-max)		8.45 (1.11-75.54)	5.13 (1.90-278.33)	0.764
Decrease of serum Anti-Tg Ab levels		p<0.001	p=0.277	
Tg 1 level Median (min-max)		6.76 (0.00-64.25)	35.55 (0.14-619.30)	<0.001
Tg1 level	<10ng/ml	34	3	0.006
	≥10 ng/ml	23	12	
Decrease of serum		<0.001	0.021	0.006
	Tg levels	<0.001	0.011	

Anti-TgAb: Serum anti-thyroglobulin antibody, Tg: thyroglobulin , Anti-Tg Ab 1 and Tg 1: The measurement before ablation therapy, Anti-Tg Ab 2 : The measurement before whole body 131I scan at 6–12 months after ablation

of the clinical and demographic parameters (Table 1). Comparison of Antithyroglobulin Antibody and Thyroglobulin Outcomes Anti-Tg antibody was positive in 41 of 113 (36%) subjects and negative in 72 (64%) subjects before RAI ablation. There was no statistically significant difference between groups in terms of anti-Tg antibody positivity. There were no differences between groups in terms of anti-Tg Ab 1 and anti-Tg Ab 2 levels. When the groups were compared in terms of anti-Tg Ab decline after the treatment, there was a significant decrease in Group 1 (p <0.001), while no significant decrease in Group 2 (p = 0.277) was observed.

The evaluation of the decline in Tg values after the treatment showed a significant difference between both groups (Table 2). There was no significant correlation between tumor size and anti-Tg 1 values. Also, there was no significant correlation between tumor size and decreased anti-Tg (Anti Tg2-Anti Tg1) levels.

Discussion

In this study, we examined the results of 113 patients with DTC who received RAI ablation therapy after total thyroidectomy. The anti-Tg Ab positivity rate in our study was 36%. The literature describes different anti-Tg Ab positivity rates in DTC patients [4, 10, 11]. These rates vary from 6.2% to 35%. The different prevalences of anti-Tg Ab rates in DTC may reflect differences in methodological sensitivities and specificities and also the threshold range for a “positive” Tg Ab in the studies. TgAb levels are higher in DTC patients than in the general population. For this reason, It is thought that Hashimoto thyroiditis is related to thyroid cancer [10,12]. TgAb may interfere with thyroglobulin (Tg) and may cause falsely low or undetectable Tg level [13]. This rate was 25% in the study by Dufour [14]. For this reason, the role of anti-Tg for follow-up in anti-Tg positive DTC patients is under debate. The studies were conducted to determine whether anti-Tg Ab level may be a marker

of prognosis [1, 4, 9-11, 15-17]. In a study by Jo et al. which retrospectively evaluated 1171 (254 with anti-tg positive) DTC patients, a positive preoperative serum anti-Tg Ab level was associated with worse tumor features (higher lymphatic invasion and lymph node metastasis) but rarely displayed poor prognosis [10]. A recent study, reported by Kuo et al. included 1206 (75 with anti-Tb positive) patients, Study results revealed that during the disease course, positive anti-Tg Ab level was not being related to the prognosis in PTC patients [4]. In our study, patients were assigned into two groups, as successful (Group 1) and unsuccessful (Group 2), according to the results of ablation therapy. No significant difference was established in the groups in terms of anti-Tg levels and anti-Tg Ab positivity. We speculate that the result of our study may be related to the small sample size. According to these results, we think further research is needed on this subject.

There are some studies in the literature regarding the usefulness of anti-Tg Ab in the follow-up of the patients [1, 2, 4, 9, 11, 18]. These studies emphasized that changes in anti-Tg Ab during 6-12 months after ablation period may be an indicator of recurrence. In our study, we examined whether there was a significant decrease in anti-Tg Ab levels within 6-12 months after ablation therapy. There was a significant decrease in patients with successful ablation therapy, but there was no significant decrease in unsuccessful patients. In the review reported by Verburg and colleagues, a minimum waiting period of 6 months is suggested for considering an increase in anti-Tg Ab to be an indicator of potentially progressive disease. However, they reported that anti-Tg Ab levels may be interpreted as a sign of the remission of the disease over the months following the ¹³¹I therapy [19]. American Thyroid Association (ATA) guidelines emphasized that if the patients who were initially positive for anti-Tg antibodies, thereafter become negative but subsequently have rising levels of anti-Tg Ab, repeated or progressive disease should be suspected. Declining levels of anti-Tg Ab may imply successful therapy [20].

Serum Tg level is an assay routinely used to follow DTC patients who have undergone ablation therapy and total thyroidectomy. Studies revealed that Tg values measured after total thyroidectomy or before RAI ablation therapy contribute to the risk stratification. It was also emphasized that Tg values can be used for prediction of treatment success [21- 24]. Tg 1 levels were statistically different between the two groups in our study. In the ablation successful group, Tg 1 levels were lower. Furthermore, although there was a limited number of patients when the threshold for Tg 1 is taken as 10; the achievement rate was higher in patients with Tg 1 <10 ng / mL when compared to pre-treatment values. We evaluated the decrease in serum Tg level, and there was a significant decrease in patients with or without anti-Tg positive in both Group 1 and Group 2. However, there was a significant decrease in the anti-Tg level only in Group 1 patients who benefited from ablation therapy. The limitation of this study was the low number of anti-Tg positive patients. We believe that further studies with more patients will contribute to this area.

In conclusion, we believe that a reduction in the anti-Tg Ab level, measured between 6 and 12 months after the ablation, may be

indicative of treatment success. For this reason, the serum level of anti-Tg Ab can be a reliable tool in the evaluation of ablation success.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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